



ATTORNEY DOCKET NO.: 0492611-0505 (MIT 9991 US NATL)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Chau, et al. Examiner:  
Serial No.: 10/668,045 Art Unit:  
Filing Date: September 22, 2003  
Title: Polymer-Linker-Drug Conjugates for Targeted Drug Delivery

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

**STATEMENT**

Pursuant to the duty of disclosure under 37 C.F.R. §§1.56, 1.97 and 1.98, Applicant requests consideration of this Information Disclosure Statement.

Type of Statement

The present Information Disclosure Statement is:

- [X] An *original* Information Disclosure Statement; or  
[ ] A *supplemental* Information Disclosure Statement.

<b>Certificate of Mailing</b>	
I certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.	
<u>12-17-03</u>	<u>Sandra Saccoccia</u>
Date	Signature
<u>Sandra Saccoccia</u>	
Typed or Printed Name of person signing certificate	

Compliance with 37 CFR § 1.97

The present Information Disclosure Statement is being filed:

- ☒ Pursuant to 37 CFR § 1.97(b); no fee or certification is required:
  - ☒ Within three months of the filing date of a national application other than a continued prosecution application under § 1.53(d);
  - ☐ Within three months of the date of entry of the national stage as set forth in § 1.491 in an international application;
  - ☒ Before the mailing of a first Office action on the merits; or
  - ☐ Before the mailing of a first Office action after the filing of a request for continued examination under § 1.114.
- ☐ Pursuant to 37 CFR § 1.97(c) after the dates listed above but before the mailing date of any of a final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application; Applicant hereby *either*:
  - ☐ Certifies that *either*:
    - ☐ each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or
    - ☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the

knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.; or

☐ Includes herewith the fee set forth in § 1.17(p).

☐ Pursuant to 37 CFR § 1.97(d), after the mailing date of any final action under § 1.113, a notice of allowance under § 1.311, or an action that otherwise closes prosecution in the application; Applicant hereby *both*:

☐ Certifies that *either*:

☐ each item of information contained in the information disclosure statement was first cited in any communication from a foreign patent office in a counterpart foreign application not more than three months prior to the filing of the information disclosure statement; or

☐ That no item of information contained in the information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and, to the knowledge of the person signing the certification after making reasonable inquiry, no item of information contained in the information disclosure statement was known to any individual designated in § 1.56(c) more than three months prior to the filing of the information disclosure statement.; and

☐ Includes herewith the fee set forth in § 1.17(p).

Content of the Information Disclosure Statement

Applicant hereby makes of record in the above-identified application the reference(s) listed on the attached form PTO-1449 (modified). The order of presentation of the references should not be construed as an indication of the importance of the references.

Applicant includes copies of references as indicated below:

☒ A copy of each cited reference not indicated with an asterisk is included;

☐ Copies of references indicated with an asterisk on the attached form PTO-1449 are not included pursuant to 37 CFR § 1.98(d) because they were previously provided to the United States Patent Office in an Information Disclosure Statement that complies with 37 CFR § 1.98(a)-(c) and was submitted in the following patent application that is relied upon in the present case for an earlier effective filing date under 35 USC § 120:

Serial Number	Filing Date	Status

☐ Copies of English translations of one or more non-English references are included.

Applicant hereby makes the following additional information of record in the above-identified application:

Applicant certifies that the Information Disclosure Statement *either*:

☐ Does not contain non-English language citations;

☐ Does contain non-English language citations, of which the following is a concise explanation:

☐ Includes one or more translations of a non-English citation.

## Remarks

The submission of this Information Disclosure Statement should not be construed as a representation that a search has been made.

The submission of this Information Disclosure Statement shall not be construed to be an admission that the information cited in the statement is, or is considered to be, material to patentability as defined in § 1.56(b) .


The submission of this Information Disclosure Statement shall not be construed as a representation that the information cited in the Statement is, or is considered to be, in fact, prior art as defined by 35 U.S.C. §102.

It is respectfully requested that:

1. The Examiner consider completely the cited information, along with any other information, in reaching a determination concerning the patentability of the present claims;
2. The enclosed form PTO-1449 be signed by the Examiner to evidence that the cited patent(s) and publication(s) has (have) been fully considered by the Patent and Trademark Office during the examination of this application; and
3. The citations for the patent(s) and publication(s) be printed on any patent which issues from this application.

Notwithstanding any statements by Applicants, the Examiner is urged to form his or her own conclusions regarding the relevance of the cited reference(s).

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'C. Lyon', is written over a horizontal line.

Charles E. Lyon, D.Phil.

Agent for Applicant

Limited Recognition Under 37 CFR §10.9(b)

CHOATE, HALL & STEWART  
Exchange Place  
53 State Street  
Boston, Massachusetts 02109  
(617) 248-5000  
(617) 248-4000

Dated: December 17, 2003

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ATTORNEY DOCKET NO.: 0492611-0505 (MIT 9991 US NATL)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicant: Chau, et al. Examiner: NYA  
Serial No.: 10/668,045 Art Unit: NYA  
Filing Date: September 22, 2003  
Title: Polymer-Linker-Drug Conjugates for Targeted Drug Delivery

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:


**TRANSMITTAL LETTER**

Enclosed are the following documents:

1. Form PTO-1449 (3 pages);
2. Information Disclosure Statement (6 pages);
3. Cited Art (35 documents);
4. Statement of Limited Recognition (1 page); and
5. Return Postcard

If any additional fees are required to be paid or if any overpayment has been made, please charge same to Deposit Account No. 03-1721.

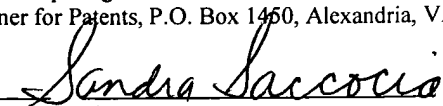
Respectfully submitted,

  
\_\_\_\_\_  
Charles E. Lyon, D.Phil.  
Agent for Applicant  
Limited Recognition Under 37 CFR §10.9(b)

Choate, Hall & Stewart  
Exchange Place  
53 State Street  
Boston, MA 02109  
(617) 248-5000

Dated: December 17, 2003

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Certificate of Mailing	
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Sandra Saccoccia	
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Form PTO-1449 (REV. 8-83) U.S. Department of Commerce Patent and Trademark Office <b>INFORMATION DISCLOSURE STATEMENT</b> (Use several sheets if necessary)		Atty. Docket: 0492611-0505		In re Application No. 10/668,045	
		Applicant: Chau et al.			
		Filing Date: September 22, 2003		Group: NYA	

<b>U.S. PATENT DOCUMENTS</b>					
Examiner's Initials	U.S. Patent No.	Applicant	Issue Date	Class	Subclass
	6,372,205	Duncan et al.	April 16, 2002	424	78.17
	6,361,774	Griffiths et al.	March 26, 2002	424	178.1
	5,037,883	Kopecek et al.	August 6, 1991	525	54.1

<b>U.S. PATENT APPLICATIONS</b>					
Examiner's Initials:	Serial Number:	Applicant:	Filing Date:	Group:	Art Unit:

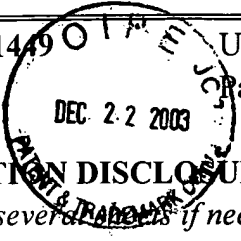
  

<b>FOREIGN PATENT DOCUMENTS</b>					
Examiner's Initials	Document No.	Country	Date	Translation	
				Yes	No

<b>OTHER DOCUMENTS</b>	
Examiner's Initials	Citation (Including Author, Title, Date, Pertinent Pages, Etc.)
	Bagshawe, et al., "First Clinical Experience with ADEPT", <i>Adv. Drug. Delivery Rev.</i> 22(3): 365-367, 1996.
	Burger, et al., "Pre-Clinical Evaluation of a Methotrexate-Albumin Conjugate (MTX-HSA) In Human Tumor Xenografts in Vivo", <i>International Journal of Cancer</i> , 92: 718-724, 2001.
	Chau, et al., "Important Factors in Designing Targeted Delivery of Cancer Therapeutics via MMP-2 Mediation", Abstract from 2nd International Symposium on Tumor Targeted Delivery Systems, September 2002.
	Chau, et al., "A Novel Polymer-Peptide-Drug Conjugate for Tumor Targeting via MMP-2 Mediation". Abstract from 7th US-Japan Symposium on Drug Delivery Systems, December 2003.
	Danhauser-Riedel, et al., "Phase-I Clinical and Pharmacokinetic Trial of Dextran Conjugated Doxorubicin (AD-70, DOX-OXD)", <i>Investigational New Drugs</i> , 11(2-3): 187-195, 1993.
	Duncan, et al., "Preclinical Evaluation of Polymer-Bound Doxorubicin", <i>J. Controlled Release</i> , 19: 331-346, 1992.
	Duncan, et al., "Design of Oligopeptide Side Chains in Poly N-(2-Hydroxypropyl) Methacrylamide Copolymers to Promote Efficient Degradation by Lysosomal Enzyme", <i>Makromol. Chem.</i> 184: 1997-2008, 1983.



Form PTO-1449  U.S. Department of Commerce (REV. 8-83) Patent and Trademark Office		Atty. Docket: 0492611-0505	In re Application No. <b>10/668,045</b>
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	Duncan, et al., "Polymer-Drug Conjugates, PDEPT and PELT: Basic Principles for Design and Transfer from the Laboratory to Clinic", <i>Journal of Controlled Release</i> , <b>74</b> (1-3): 135-146, 2001.		
	Flanagan, et al., "Evaluation of Protein-N-(2-Hydroxypropyl) Methacrylamide Copolymer Conjugates as Targeted Drug-Carriers. 2. Body Distribution of Conjugates Containing Transferrin, Antitransferrin Receptor Antibody or Anti-Thy 1.2 Antibody and Effectiveness of Transferrin-Containing Daunomycin Conjugates Against Mouse L1210 Leukaemia in Vivo", <i>Journal of Controlled Release</i> , <b>18</b> : 25-38, 1992.		
	Garsky, et al., "The Synthesis of a Prodrug of Doxorubicin Designed to Provide Reduced Systemic Toxicity and Greater Target Efficacy", <i>Journal of Medicinal Chemistry</i> , <b>44</b> : 4216-4224, 2001.		
	Hoes, et al., "Biological Properties of Adriamycin Bound to Biodegradable Polymeric Carriers", <i>J. Controlled Release</i> , <b>23</b> : 37-54, 1993.		
	Matsumura, et al., "A New Concept for Macromolecular Therapeutics in Cancer Chemotherapy: Mechanism of Tumorotropic Accumulation of Proteins and the Antitumor Agent Smancs", <i>Cancer Research</i> , <b>46</b> : 6387-6392, 1986.		
	Munechika, et al., "Tissue Distribution and Macromolecular Conjugate, Adriamycin Linked to Oxidized Dextran, in Rat and Mouse Bearing Tumor Cells", <i>Biol. Pharm. Bull.</i> <b>17</b> (9): 1193-1198, 1994.		
	Noguchi, et al., "Tumor Localization and in vivo Antitumor Activity of the Immunoconjugate Composed of Anti-Human Colon Cancer Monoclonal Antibody and Mitomycin C-Dextran Conjugate", <i>Japanese J. Cancer Res.</i> <b>82</b> : 219-226, 1991.		
	Nogusa et al., "Distribution Characteristics of Carboxymethylpullulan-Peptide Doxorubicin Conjugates in Tumor-Bearing Rats: Different Sequences of Peptide Spacers and Doxorubicin Contents", <i>Biol. Pharm. Bull.</i> <b>23</b> (5): 621-626, 2000.		
	Nogusa, et al., Antitumor Effects and Toxicities of Carboxymethylpullulan-Peptide-Doxorubicin Conjugates", <i>Biol. Pharm. Bull.</i> <b>20</b> (10): 1061-1065, 1997.		
	Park, et al., "Fibroblast Activation Protein, A Dual Specificity Serine Protease Expressed in Reactive Human Tumor Stromal Fibroblasts", <i>J. Biol. Chem.</i> <b>274</b> (51): 36505-36512, 1999.		
	Pechar, et al., "Conjugates of Antibody-Targeted PEG Multiblock Polymers with Doxorubicin in Cancer Therapy", <i>Macromolecular Bioscience</i> , <b>3</b> : 364-372, 2003.		
	Pimm, et al., "Gamma Scintigraphy of the Biodistribution of I-123-Labelled N-(2-Hydroxypropyl) Methacrylamide Copolymer-Doxorubicin Conjugates in Mice with Transplanted Melanoma and Mammary Carcinoma", <i>J. Drug Targeting</i> , <b>3</b> (5): 375, 1996.		
	Putnam, et al., "Polymer Conjugates with Anticancer Activity", <i>Advances in Polymer Sciences</i> , <b>122</b> : 55-123, 1995.		

<b>Form PTO-1449</b> (REV. 8-83)		U.S. Department of Commerce Patent and Trademark Office	
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		Group: NYA	

Examiner's Initials	Citation (Including Author, Title, Date, Pertinent Pages, Etc.)
	Rejmanova, et al., "Stability in Plasma and Serum of Lysosomally Degradable Oligopeptide Sequences in N-(2-Hydroxypropyl)Methacrylamide Copolymers", <i>Biomaterials</i> , 6: 45-48, 1985.
	Rejmanova, et al., "Degradation of Oligopeptide Sequences in N-(2-Hydroxypropyl) Methacrylamide Copolymers by Bovine Spleen Cathepsin B", <i>Makromol. Chem.</i> 184: 2009-2020, 1983.
	Seftor, et al., "Chemically Modified Tetracyclines Inhibit Human Melanoma Cell Invasion and Metastasis" <i>Clinical &amp; Experimental Metastasis</i> , 16(3): 217-225, 1998.
	Seymour, et al., "The Pharmacokinetics of Polymer-Bound Adriamycin", <i>Biochemical Pharmacology</i> , 39(6): 1125-1131, 1990.
	Seymour, et al., "Hepatic Drug Targeting: Phase I Evaluation of Polymer-Bound Doxorubicin", <i>Journal of Clinical Oncology</i> , 20: 1668-1676, 2002.
	Song, et al., "Pharmacokinetic Characteristics and Antitumor Activity of the N-Succiny-Chitosan-Mitomycin C Conjugate and the Carboxymethyl-Chitin-Mitomycin C Conjugate", <i>Biol. Pharm. Bull.</i> 16(1): 48-54, 1993.
	Takakura, et al., "Macromolecular Carrier Systems for Targeted Drug Delivery: Pharmacokinetic Considerations on Biodistribution", <i>Pharmaceutical Res.</i> , 13(6), 820-831, 1996.
	Tang, et al., "Binding and Cytotoxicity of HPMa Copolymer Conjugates to Lymphocytes Mediated by Receptor-Binding Epitopes", <i>Pharmaceutical Research</i> , 20: 360-367, 2003.
	Trouet, et al., "A Covalent Linkage Between Daunorubicin and Proteins that is Stable in Serum and Reversible by Lysosomal Hydrolases, as Required for A Lysosomotropic Drug-Carrier Conjugate: In Vitro and In Vivo Study", <i>Proc. Natl. Acad. Sci. USA</i> , 79: 626-629, 1982.
	Ulbrich, et al., "Poly(Ethylene Glycol)s Containing Enzymatically Degradable Bonds", <i>Makromol. Chem.</i> 187: 1131-1144, 1986.
	Yokoyama, et al., "Toxicity and Antitumor Activity Against Solid Tumors of Micelle-Forming Polymeric Anticancer Drug and its Extremely Long Circulation in Blood", <i>Cancer Research</i> , 51: 3229-3236, 1991.
	Ziober, et al., "Type I Collagen Degradation by Invasive Oral Squamous Cell Carcinoma", <i>Oral Oncology</i> , 36(4): 365-372, 2000.

<b>EXAMINER</b>	<b>DATE CONSIDERED</b>
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EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.